REMARKS

Claims 2 & 5 are in the case. Claims 3 and 4 are being cancelled by this amendment.

The courtesies extended by Examiner Fay and SPE Krass during the personal interview with co-inventor Dr. Goldberg and the undersigned on April 10, 2008, are acknowledged with appreciation. The substance of the interview will be discussed below.

Claims 2 & 5 were rejected under 35 U.S.C. 103 over Physician's Desk Reference (PDR) in view of Wu et al. and Caldwell et al. The basis of the rejection was that it is known that drowsiness is a symptom associated with anesthetics (Wu), that modafinil is a known "wakefulness agent" (PDR), and modafinil is known for sustaining alertness and performance of aviators (Caldwell). From these teachings the examiner held that it would have been obvious that modafinil would be useful to improve a patient's recovery from anesthesia.

A declaration under 37 CFR 1.132 of Paul Frederick White, Ph.D., M.D., was filed in response to the office action of June 19, 2007, in order to rebut the prima facie obviousness rejection. Dr. Paul White is an independent person of extraordinary skill in this art, of impeccable credentials in the field to which this invention is directed, who stated in his declaration his opinion that the improvements discovered by the present inventors from the administration of modafinil to improve recovery from anesthesia were unexpected. Dr. White has no financial interest in the present patent application and is not employed by the assignee or any other entity having interest in the present patent application. The Examiner found the declaration to be unpersuasive without any supporting evidence to demonstrate that modafinil would not be effective in reducing the symptoms of general anesthesia such as drowsiness and loss of alertness.

Under this theory of the present rejection, any anti-narcoleptic would be useful to improve a patient's recovery from anesthesia. It is very important to note that the examiner has not cited any reference at all showing anti-narcoleptics being used for improving patients' recovery from anesthesia. In fact, anti-narcoleptics in general have not been used following anesthesia to improve recovery, according to paragraph 13 of the Paul Frederick White Declaration under 37 CFR 1.132.

At the personal interview, applicants explained the difference in mechanism between narcolepsy and anesthesia-induced sleep. It is currently believed that anesthesia works by a cell death mechanism, which is different from the mechanism of the narcolepsy and other previously known uses of modafinil. The GABA system, including catecholamine, melatonine, and dopamine, are stimulated by anethetics to anesthestize a patient. Applicants explained that anesthesia induced, i.e., chemically induced, sleep is very different from the naturally induced sleep for which modafinil was known. None of the known uses of modafinil were for counteracting any chemically induced sleep, whether anesthesia induced or other drug induced.

Other drugs such as Ritalin and Permoline (see, e.g., Percheson and Rivera articles attached hereto as Exhibits E and F) and amphetamines have been tried but they all have such serious problems that they would not be used other than experimentally. Ritalin is known to act on the catecholamine system. The precise mechanism of modafinil activity is unknown according to the label in PDR, but modafinil works by a different profile than that of Ritalin. Modafinil is not a dopamine receptor agonist or antagonist.

Dr. Goldberg pointed out that at the largest annual anesthesia convention where papers were presented and posters were exhibited, the poster by applicants won the first prize that year and that hoards of people were excited about the discovery, assumedly because it would solve a very long-felt need. The meeting Dr. Goldberg was referring to was the 2004 annual meeting of the International Anesthesia Research Society in Orlando, Florida (April 2004) where the Abstract describing the present invention won "best of meeting" and "best of section" awards. Applicants are searching for a publication documenting these two prestigious awards and may supply such publication if found, but attached as Exhibits A and B are photographs of the two awards, one a red Best of Section ribbon and one a yellow Best of Meeting ribbon received during the 78th Clinical and Scientific Congress of the International Anesthesia Research Society, March 27-31, 2004, where applicants paper, attached as Exhibit C, was one of 282 papers presented, abstracts of which are set forth in the Abstracts of Papers Supplement, published online only, attached as Exhibit D. This recognition by applicants' peers is a secondary indicia negativing *prima facie* obviousness under the *Graham v. John Deere* test, upheld and cited favorably by the U.S. Supreme Court in *KSR Int'l v. Teleflex.*

The excerpt from the cited 2002 PDR includes product information for Provigil brand of modafinil tablets, describing its mechanism of action, pharmacology, pharmacokinetics, precautions, clinical trial data, indications and usage, contraindications, cautions, interactions, uses, adverse reactions, dosage, administration, etc., in great detail. One skilled in the art reading this PDR excerpt would know how and when to prescribe and use modafinil, but would not be led to off label uses. In general, the PDR describes the use of modafinil as a narcoleptic but does not describe any use in connection with the problem to which the present invention is addressed, the problem of undesired and unintended cognitive dysfunction following a medical procedure where anesthetic was used on the patient.

The prior art teaches what was previously known about the modanifil's many uses and mechanism of action, but nowhere describes any use relating to recovery from anesthesia. The facts that modafinil has been so extensively researched by others and as reported in the cited publications relating to its uses, and that no use relating to recovery from anesthesia was described in the literature actually teaches away from the present invention. One skilled in the medical arts would have expected all known and possible uses to have been described in either the patent literature, medical literature, or the PDR.

The surprising and unexpected utility of modafinil to reduce symptoms related to recovery from anesthesia were demonstrated clinically and the experimental data were reported in the specification at Tables 1 and 2 on pages 5-8. Further data is included in the attached published article authored by the inventors and others.

During the personal interview, the examiners suggested certain amendments to the claims which are being made herewith. It was agreed that the prior art did not appear to suggest reducing cognitive dysfunction symptoms caused by general anesthesia and that such a claim would probably overcome the obviousness rejection when submitted in conjunction with the prior art showing Ritalin and other drugs being tried but not being useful, and with reference to the comparative data in the specification and the enclosed article by the inventors.

Applicants have effectively rebutted the prima facie obviousness rejection made in the last office action by demonstrating that the invention was unexpected and surprising.

For these reasons, reconsideration and withdrawal of the rejection of the present claims is solicited.

Respectfully submitted

COZEN O'CONNOR

/Michael B Fein/

By: Michael B. Fein
Reg. 25,333

1900 Market Street
Philadelphia, PA 19103
Phone: 215 665-4622
Fax: 215-701-2246